

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Crooke et al.

Confirmation No.: 6394

Patent No.: 7,511,131

Art Unit: 1636

Issued: March 31, 2009

For: Antisense Modulation of
Apolipoprotein B Expression

Attorney Docket No.: 12207-002-999

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT UNDER 37 C.F.R. § 3.73(b)

Genzyme Corporation (hereinafter "Genzyme"), a corporation of the State of Massachusetts, having a place of business at 500 Kendall Street, Cambridge, Massachusetts 02142, states that it is the assignee of the entire right, title, and interest in the above-identified U.S. patent by virtue of an assignment from the inventor(s). The assignment has been submitted to the United States Patent and Trademark Office for recordation, which a copy thereof is attached.

**REVOCATION OF PREVIOUS AND POWER OF ATTORNEY AND
NEW POWER OF ATTORNEY BY ASSIGNEE**

Genzyme hereby revokes any and all previous powers of attorney given in the above-identified patent and hereby appoints the registered practitioners of JONES DAY at Customer Number **90469** to make and to transact all business in the Patent and Trademark Office connected therewith.

REQUEST FOR CHANGE OF CORRESPONDENCE ADDRESS

Please send all future correspondence and direct telephone calls to Customer Number
90469.

The undersigned (whose title is supplied below) is authorized to act on behalf of the
assignee.

ASSIGNEE: Genzyme Corporation

Date: 9/1/09 Signature: MKS Shafmaster
Typed Name: Madge K. Shafmaster
Position/Title: Senior Vice President and Chief Patent
Counsel



UNITED STATES PATENT AND TRADEMARK OFFICE

UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND
DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE



500611633A

AUGUST 05, 2008

PTAS

ISIS PHARMACEUTICALS, INC.
1896 RUTHERFORD ROAD
CARLSBAD, CA 92008

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 571-272-3350. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, MAIL STOP: ASSIGNMENT SERVICES BRANCH, P.O. BOX 1450, ALEXANDRIA, VA 22313.

RECORDATION DATE: 08/04/2008

REEL/FRAME: 021336/0565
NUMBER OF PAGES: 9

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).
DOCKET NUMBER: GENZYME ASSIGNMENT

ASSIGNOR:

ISIS PHARMACEUTICALS, INC.

DOC DATE: 07/17/2008

ASSIGNEE:

GENZYME CORPORATION
500 KENDALL STREET
CAMBRIDGE, MASSACHUSETTS 02142

SERIAL NUMBER: 09920033

FILING DATE: 08/01/2001

PATENT NUMBER:

ISSUE DATE:

TITLE: ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION

SERIAL NUMBER: 10135985

FILING DATE: 04/30/2002

PATENT NUMBER:

ISSUE DATE:

TITLE: ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION

021336/0565 PAGE 2

SERIAL NUMBER: 10147196 FILING DATE: 05/15/2002
PATENT NUMBER: 7407943 ISSUE DATE: 08/05/2008
TITLE: ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION

SERIAL NUMBER: 11969096 FILING DATE: 01/03/2008
PATENT NUMBER: ISSUE DATE:
TITLE: ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION

SERIAL NUMBER: 60426234 FILING DATE: 11/13/2002
PATENT NUMBER: ISSUE DATE:
TITLE: INHIBITION OF APOB-100 FOR THE TREATMENT OF HYPERLIPIDEMIAS

SERIAL NUMBER: 10712795 FILING DATE: 11/13/2003
PATENT NUMBER: ISSUE DATE:
TITLE: ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION

SERIAL NUMBER: 10920612 FILING DATE: 08/17/2004
PATENT NUMBER: ISSUE DATE:
TITLE: ANTISENSE MODULATION OF APOLIPOPROTEIN B-EXPRESSION

SERIAL NUMBER: 10916218 FILING DATE: 08/10/2004
PATENT NUMBER: ISSUE DATE:
TITLE: COMPOSITIONS AND METHODS FOR MODULATING LIPOPROTEIN AND CHOLESTEROL
LEVELS IN HUMANS

SERIAL NUMBER: 60612831 FILING DATE: 09/23/2004
PATENT NUMBER: ISSUE DATE:
TITLE: METHODS FOR MODULATING LIPOPROTEIN AND CHOLESTEROL LEVELS IN HUMANS

SERIAL NUMBER: 11200710 FILING DATE: 08/10/2005
PATENT NUMBER: ISSUE DATE:
TITLE: METHODS FOR MODULATING LIPOPROTEIN AND CHOLESTEROL LEVELS IN HUMANS

SERIAL NUMBER: 11573537 FILING DATE:
PATENT NUMBER: ISSUE DATE:
TITLE: ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION

SERIAL NUMBER: 60568825 FILING DATE: 05/05/2004
PATENT NUMBER: ISSUE DATE:
TITLE: EFFECTS OF APOLIPOPROTEIN B INHIBITION ON GENE EXPRESSION PROFILES
IN ANIMALS

SERIAL NUMBER: 11123656 FILING DATE: 05/05/2005
PATENT NUMBER: ISSUE DATE:
TITLE: EFFECTS OF APOLIPOPROTEIN B INHIBITION ON GENE EXPRESSION PROFILES
IN ANIMALS

SERIAL NUMBER: 60896914 FILING DATE: 03/24/2007
PATENT NUMBER: ISSUE DATE:
TITLE: ADMINISTERING OLIGONUCLEOTIDES

SERIAL NUMBER: 60568409 FILING DATE: 05/05/2004
PATENT NUMBER: ISSUE DATE:
TITLE: SNPS OF APOLIPOPROTEIN B AND MODULATION OF THEIR EXPRESSION

021336/0565 PAGE 3

SERIAL NUMBER: 11124020 FILING DATE: 05/05/2005
PATENT NUMBER: ISSUE DATE:
TITLE: SNPS OF APOLIPOPROTEIN B AND MODULATION OF THEIR EXPRESSION

SERIAL NUMBER: 60600785 FILING DATE: 08/10/2004
PATENT NUMBER: ISSUE DATE:
TITLE: METHODS FOR MODULATING LIPOPROTEIN AND CHOLESTEROL LEVELS IN HUMANS

SERIAL NUMBER: FILING DATE: 07/30/2002
PATENT NUMBER: ISSUE DATE:
PCT NUMBER: US0224247
TITLE: ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION

SERIAL NUMBER: FILING DATE: 05/15/2003
PATENT NUMBER: ISSUE DATE:
PCT NUMBER: US0315493
TITLE: ANTISNESE MODULATION OF APOLIPOPROTEIN B EXPRESSION

SERIAL NUMBER: FILING DATE: 11/13/2003
PATENT NUMBER: ISSUE DATE:
PCT NUMBER: US0336411
TITLE: ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION

SERIAL NUMBER: 11573537 FILING DATE:
PATENT NUMBER: ISSUE DATE:
PCT NUMBER: US0528342
TITLE: ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION

SERIAL NUMBER: FILING DATE: 03/24/2008
PATENT NUMBER: ISSUE DATE:
PCT NUMBER: US0858072
TITLE: ADMINISTERING OLIGONUCLEOTIDES

ASSIGNMENT SERVICES BRANCH
PUBLIC RECORDS DIVISION

PATENT ASSIGNMENT

Electronic Version v1.1
 Stylesheet Version v1.1

08/04/2008
 500611633

| SUBMISSION TYPE: | NEW ASSIGNMENT |
|----------------------------|---------------------|
| NATURE OF CONVEYANCE: | ASSIGNMENT |
| CONVEYING PARTY DATA | |
| Name | Execution Date |
| Isis Pharmaceuticals, Inc. | 07/17/2008 |
| RECEIVING PARTY DATA | |
| Name: | Genzyme Corporation |
| Street Address: | 500 Kendall Street |
| City: | Cambridge |
| State/Country: | MASSACHUSETTS |
| Postal Code: | 02142 |
| PROPERTY NUMBERS Total: 22 | |
| Property Type | Number |
| Application Number: | 09920033 |
| Application Number: | 10135985 |
| Application Number: | 10147196 |
| Application Number: | 11969096 |
| Application Number: | 60426234 |
| Application Number: | 10712795 |
| Application Number: | 10920612 |
| Application Number: | 10916218 |
| Application Number: | 60612831 |
| Application Number: | 11200710 |
| Application Number: | 11573537 |
| Application Number: | 60568825 |
| Application Number: | 11123656 |
| Application Number: | 60896914 |
| Application Number: | 60568409 |

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| | |
|---------------------|-----------|
| Application Number: | 11124020 |
| Application Number: | 60600785 |
| PCT Number: | US0224247 |
| PCT Number: | US0315493 |
| PCT Number: | US0336411 |
| PCT Number: | US0528342 |
| PCT Number: | US0858072 |

CORRESPONDENCE DATA

Fax Number: (760)603-3820

Correspondence will be sent via US Mail when the fax attempt is unsuccessful.

Phone: 760-603-2553

Email: leames@isisph.com

Correspondent Name: Isis Pharmaceuticals, Inc.

Address Line 1: 1896 Rutherford Road

Address Line 4: Carlsbad, CALIFORNIA 92008

ATTORNEY DOCKET NUMBER:

GENZYME ASSIGNMENT

NAME OF SUBMITTER:

Laura Eames

Total Attachments: 7

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UNITED STATES PATENT AND TRADEMARK OFFICE

Facsimile Transmission

To: Name: ISIS PHARMACEUTICALS, INC.
 Company: 1896 RUTHERFORD ROAD
 Fax Number: 17606033820
 Voice Phone:

From: Name: ASSIGNMENT SERVICES BRANCH
 Voice Phone: 571-272-3350

37 C.F.R. 1.6 sets forth the types of correspondence that can be communicated to the Patent and Trademark Office via facsimile transmissions. Applicants are advised to use the certificate of facsimile transmission procedures when submitting a reply to a non-final or final Office action by facsimile (37 CFR 1.8(a)).

Fax Notes:

| Pg# | Description |
|-----|---------------------------|
| 1 | Cover Page |
| 2 | 636.TXT |
| 5 | Document 1, Batch 1360253 |

USPTO ASSIGNMENT SYSTEM PROCESSING

Date and time of transmission: Wednesday, August 06, 2008 1:20:50 PM
Number of pages including this cover sheet: 06

EXHIBIT E
FORM OF PATENT ASSIGNMENT
PATENT ASSIGNMENT

WHEREAS, Isis Pharmaceuticals, Inc. ("Assignor"), a Delaware corporation with an address of 1896 Rutherford Road, Carlsbad, California 92008, is the owner of all rights, title, and interests in and to the patents and patent applications shown on the attached **Exhibit 1** (the "Patents"); and

WHEREAS, Genzyme Corporation ("Assignee"), a Massachusetts corporation with an address of 500 Kendall Street, Cambridge, Massachusetts 02142, desires to acquire the entire right, title, and interest in and to the Patents and all the inventions and discoveries disclosed in the Patents (the "Inventions");

NOW THEREFORE, be it known that effective as of July 17, 2008, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Assignor hereby sells, assigns, transfers, and sets over unto Assignee (1) the entire right, title, and interest in all countries throughout the world in and to said Patents and Inventions, including any renewals, revivals, reissues, reexaminations, extensions, continuations, continuations-in-part, and divisions of said Patents and any substitute applications therefor; (2) the entire right to file patent applications ("New Applications") in the name of Assignee or its designee, or in the name of Assignor at Assignee's or its designee's election, on the aforesaid Inventions in all countries of the world; (3) the entire right, title, and interest in and to any patent which issued and may issue on the Inventions in any country, and any renewals, revivals, reissues, reexaminations, and extensions thereof, and any patents of confirmation, registration, and importation of the same; (4) the right to sue and recover for, and the right to profits or damages due or accrued in connection with, any and all past, present, or future infringements of the Patents and Inventions; and (5) the entire right, title, and interest in all convention and treaty rights of all kinds, including without limitation all rights of priority in any country of the world, in and to the above Patents and Inventions;

AND, Assignor hereby authorizes and requests the competent authorities to grant and to issue any and all patents on the Inventions throughout the world to Assignee, its successors, or assigns, whose rights, title, and interests in such patents are the same as would have been held and enjoyed by Assignor had this assignment, sale, and transfer not been made.

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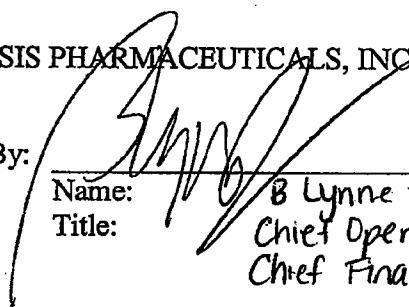
IN WITNESS WHEREOF, the Assignor has caused this Patent Assignment to be duly executed by its officer thereunto duly authorized as of the 17th day of July, 2008.

ISIS PHARMACEUTICALS, INC.

By:

Name:

Title:

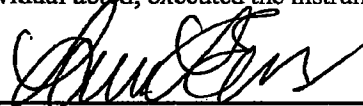

B Lynne Parshall
Chief Operating Officer and
Chief Financial Officer

STATE OF California

COUNTY OF San Diego

)
: ss.:
)

On the 17 day of July 2008 before me the undersigned, personally appeared B. Lynne Parshall, personally known to me or proved to me on the basis of satisfactory evidence to be the individual whose name is subscribed to the within instrument and acknowledged to me that he executed the same in his capacity, and that by his signature on the instrument, the individual, or the person upon behalf of which the individual acted, executed the instrument.



Notary Public



Acknowledgement of Assignee:

GENZYME CORPORATION

By: 

Name: Thomas J. DesRosier

Title: Senior Vice President, General
Counsel, Chief Legal Officer

Com.
STATE OF Massachusetts

)
: ss.:

COUNTY OF MIDDLESEX

)
On the 22 day of July, 2008, before me the undersigned, personally appeared
Thomas J. DesRosier, personally known to me or proved to me on the basis of satisfactory
evidence to be the individual whose name is subscribed to the within instrument and acknowledged to me
that he executed the same in his capacity, and that by his signature on the instrument, the individual, or
the person upon behalf of which the individual acted, executed the instrument.

Mary Ellen Hamilton
Notary Public



MARY ELLEN HAMILTON
Notary Public
Commonwealth of Massachusetts
My Commission Expires
June 11, 2010

Exhibit 1

| | <u>Isis Docket #</u> | <u>Country/Treaty</u> | <u>Patent/ Application #</u> | <u>Title</u> | <u>Issue Date</u> |
|--|-----------------------------|-------------------------------|-----------------------------------------|-----------------------------------------------------------|--------------------------|
| | ISPH-0592 | United States | 09/920,033 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | ISPH-0663 | United States | 10/135,985 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | ISPH-0688 | Patent Cooperation Treaty | PCT/US02/24247 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | ISPH-0688AU | Australia | 2002326481 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | ISPH-0688CA | Canada | 2,455,228 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | ISPH-0688EP | European Patent Convention | 2761201.9 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | ISPH-0688JP | Japan | 2003-517078 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | ISPH-0664 | United States | 10/147,196 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | [ALLOWED] |
| | ISPH-0664US.C1 | United States | 11/969,096 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | ISPH-0664WO | Patent Cooperation Treaty | PCT/US03/15493 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | DOC-0216 | United States | 60/426,234 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | DOC-0216US | United States | 10/712,795 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | DOC-0216US.C1 | United States | 10/920,612 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | DOC-0216US.P1 | United States | 10/916,218 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | DOC-0216WO | Patent Cooperation Treaty | PCT/US03/036411 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | DOC-0216AU | Australia | 2003294281 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | DOC-0216CA | Canada | 2,505,801 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | DOC-0216EP | European Patent Convention | 3789763.4 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | DOC-0216IN | India | 1218/CHENP/2005 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |

| | <u>Docket #</u> | <u>Country/Treaty</u> | <u>Patent/ Application #</u> | <u>Title</u> | <u>Issue Date</u> |
|--|-----------------|-------------------------------|----------------------------------|-------------------------------------------------------------------------------------------|-------------------|
| | DOC-0216IN.D1 | India | TBD | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | DOC-0216JP | Japan | 2005-507169 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | DOC-0216ZA | South Africa | 2005/03690 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | BIOL0045US.L | United States | 60/600,785 | METHODS FOR MODULATING LIPOPROTEIN AND CHOLESTEROL LEVELS IN HUMANS | N/A |
| | BIOL0045US.L2 | United States | 60/612,831 | METHODS FOR MODULATING LIPOPROTEIN AND CHOLESTEROL LEVELS IN HUMANS | N/A |
| | BIOL0045US | United States | 11/200,710 | METHODS FOR MODULATING LIPOPROTEIN AND CHOLESTEROL LEVELS IN HUMANS | N/A |
| | BIOL0045WO | Patent Cooperation Treaty | PCT/US2005/028342 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | BIOL0045USA | United States | 11/573,537 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | BIOL0045AU | Australia | 2005272912 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | BIOL0045CA | Canada | 2,576,860 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | BIOL0045EP | European Patent Convention | 5784428.4 | ANTISENSE MODULATION OF APOLIPOPROTEIN B EXPRESSION | N/A |
| | BIOL0039US.L2 | United States | 60/568,825 | EFFECTS OF APOLIPOPROTEIN B INHIBITION ON GENE EXPRESSION PROFILES IN ANIMALS | N/A |
| | BIOL0039US | United States | 11/123,656 | EFFECTS OF APOLIPOPROTEIN B INHIBITION ON GENE EXPRESSION PROFILES IN ANIMALS | N/A |
| | BIOL0092US.L | United States | 60/896,914 | ADMINISTERING OLIGONUCLEOTIDES | N/A |
| | BIOL0092USWO | United States | PCT/US2008/058072 | ADMINISTERING OLIGONUCLEOTIDES | N/A |
| | BIOL0021US.L | United States | 60/568,409 | SNPS OF APOLIPOPROTEIN B AND MODULATION OF THEIR EXPRESSION | N/A |
| | BIOL0021US | United States | 11/124,020 | SNPS OF APOLIPOPROTEIN B AND MODULATION OF THEIR EXPRESSION | N/A |